

electrophoresis. The protein can be isolated and purified from the culture medium of fibroblasts. Furthermore, the protein can be produced by gene engineering.--

IN THE SPECIFICATION:

Applicants have amended the specification to correct translation errors and to claim benefit of an earlier filing date. No new matter is being introduced. Please enter the following amendments:

Page 1, After the title "Novel Proteins and Methods for Producing the Proteins" and before "Field of the Invention," insert --This is a divisional application of U.S.S.N. 08/915,004, filed on August 20, 1997, which was a continuation-in-part of PCT/JP96/00374, filed on February 20, 1996, and which designated the U.S. and claims priority to JP54977/1995, filed on February 20, 1995, and JP207508/1995, filed on July 21, 1995.--

Line 8, delete "In the process, osteoblasts" and insert --Osteoblasts--;

Line 10, after "of" (first occurrence) insert --a--; delete "the progression of";

Line 11, delete "The disease" and insert --Osteoporosis--; delete "be provoked" and insert --result--;

Line 12, delete "by the condition in which" and insert --when--;

Line 14, after "causes" insert --bone--; delete "in the bone"; after "makes" delete "the bone" and insert --bone's--;

Line 15, delete the line in its entirety and insert --fragile, leading to fracture, particularly in elderly patients.--;

Line 16, delete "bedridden old people, it has" and insert --Osteoporosis has therefore--;

Line 17, delete "old" and insert --elderly--; after "people" insert --in the population--; delete "efficacious" and insert --effective--;

Line 18, delete "the";

Line 20, delete "balanced" and insert --balance of bone--;

Line 21, delete "expected to be";

Line 22, delete "are reported" and insert --reportedly--; and

Line 23, delete "to".

Page 2, Line 4, delete "Mol" and insert --Mol.--;

Line 5, after "M" insert a period ---;

Line 7, after "A" insert a period ---;

Line 9, delete "1993" and insert --1993)--;

Line 10, delete "inhibits" and insert --inhibit--;

Line 11, delete "have been paid attention and have"; and insert --have also--;

Line 14, delete "are found to";

Line 15, delete "Macrophage" and insert --macrophage--;

Line 19, delete "are found";

Line 21, delete "efficacious" and insert --effective--;

Line 23, delete "The cytokines" and insert --Cytokines--; delete "insulin like" and insert --insulin-like--; and

Line 24, delete "are now" and insert --have been--;

Page 3, Line 1, delete "effects in treatment of" and insert --effectiveness for treating--;

Line 2, delete "as a drug to care" and insert --to treat--; after "osteoporosis" (second occurrence) insert --patients--;

Line 6, delete "preparations ." and insert --preparations.--;

Line 7, delete "have been" and insert --are--;

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P.E.-

Line 8, delete "As mentioned," and insert --Since--; delete "controlled" and insert --manifest--;

Line 9, delete ". Therefore";

Line 12, delete "Disclosure" and insert --Summary--;

Line 13, delete the line in its entirety and insert --The--;

Line 14, after "factor" insert a comma --,--;

Line 15, after "(OCIF)" insert a comma --,--;

Line 22, delete "using" and insert --on--; after "pieces" insert --, which function--;
and

Line 23, delete "the".

Page 4, Line 3, delete "chromatography," and insert --chromatography:--;

Line 5, delete "The inventors, based on" and insert --After determining--;

Line 6, delete the line in its entirety and insert --OCIF, a cDNA encoding this protein
was successfully cloned.--;

Line 7, delete the line in its entirety and insert --A procedure for producing this
protein was also established--;

Line 8, delete "differentiation of osteoclasts. This" and insert --The--;

Line 9, after "has" insert --a--; delete "weights in" and insert --weight by--;

Line 10, delete "in the" and insert --under--; before "non-reducing" delete "the"; after
"conditions," (second occurrence) and insert --and--;

Line 11, delete "heparin, reduces its activity" and insert --heparin.--;

Line 12, before "to" insert --The protein's ability--; after "inhibit" insert --the--; delete
"if" and insert --is reduced when--;

Line 13, delete "lose its activity" and insert --its ability--;

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N.E.

Line 14, delete “by the treatment” and insert --is lost when treated--;

Line 15, delete “protein OCIF which is described in” and insert --OCIF protein of--;

Line 16, delete “of know factors inhibiting” and insert --other factors known to inhibit the--;

Line 18, delete “to purify” and insert --for purifying--; delete “comprising ;” and insert --comprising:--;

Line 23, before “(6)” insert --and--; and

Line 24, after "F3GA" insert --may be--.

Page 5, Line 1, delete the line in its entirety and insert --hydrophilic polymers, for example.--;

Line 2, delete “columns.” (first occurrence); delete “colomns” and insert --columns--;

Line 3, delete “accumulating the” and insert --producing--; delete “to a” and insert --in--;

Line 6, delete “the” (third occurrence);

Line 7, after “the” insert --oligonucleotide--;

Before Line 10 insert

--Brief Description of the Figures

Figure 1 shows the elution pattern of crude OCIF protein (Hiload-Q/FF pass-through fraction; sample 3) from a Hiload-S/HP column.

Figure 2 shows the elution pattern of crude OCIF protein (heparin-5PW fraction; sample 5) from a blue-5PW column.

Figure 3 shows the elution pattern of OCIF protein (blue-5PW fraction 49 to 50) from a reverse-phase column.

Figures 4A and 4B shows the SDS-PAGE of isolated OCIF proteins under reducing or non-reducing conditions. Description of the lanes:

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lane 1, 4: molecular weight marker proteins;

lane 2, 5: OCIF protein of peak 6 in figure 3;

lane 3, 6: OCIF protein of peak 7 in figure 3.

Figure 5 shows the elution pattern of peptides obtained by the digestion of pyridyl ethylated OCIF protein digested with lysylendopeptidase, on a reverse-phase column.

Figure 6 shows the SDS-PAGE of isolated natural (n) OCIF protein and recombinant (r) OCIF proteins under non-reducing conditions. rOCIF (E) and rOCIF (C) proteins were produced in 293/EBNA cells and in CHO cells, respectively. Description of the lanes:

lane 1: molecular weight marker proteins;

lane 2: a monomer type nOCIF protein;

lane 3: a dimer type nOCIF protein;

lane 4: a monomer type rOCIF (E) protein;

lane 5: a dimer type rOCIF (E) protein;

lane 6: a monomer type rOCIF (C) protein;

lane 7: a dimer type rOCIF (C) protein.

Figure 7 shows the SDS-PAGE of isolate natural (n) OCIF proteins and recombinant (r) OCIF proteins under reducing conditions. rOCIF (E) and rOCIF (C) were produced in 293 EBNA cells and in CHO cells, respectively. Description of the lanes:

lane 8: molecular weight marker proteins;

lane 9: a monomer type nOCIF protein;

lane 10: a dimer type nOCIF protein;

lane 11: a monomer type rOCIF (E) protein;

lane 12: a dimer type rOCIF (E) protein;

lane 13: a monomer type rOCIF (C) protein;

lane 14: a dimer type rOCIF (C) protein.

Figure 8 shows the SDS-PAGE of isolated natural (n) OCIF proteins and recombinant (r) OCIF proteins from which N-linked sugar chains were removed under reducing conditions. rOCIF (E) and rOCIF (C) are rOCIF proteins produced in 293/EBNA cells and in CHO cells, respectively. Description of the lanes:

lane 15: molecular weight marker proteins;

lane 16: a monomer type nOCIF protein;

lane 17: a dimer type nOCIF protein;

lane 18: a monomer type rOCIF (E) protein;

lane 19: a dimer type rOCIF (E) protein;

lane 20: a monomer type rOCIF(C) protein;

lane 21: a dimer type rOCIF(C) protein.

Figure 9 shows a comparison of OCIF and OCIF2 amino acid sequences.

Figure 10 shows a comparison of OCIF and OCIF3 amino acid sequences.

Figure 11 shows a comparison of OCIF and OCIF4 amino acid sequences.

Figure 12 shows a comparison of OCIF and OCIF5 amino acid sequences.

Figure 13 shows a standard curve determining OCIF protein concentration by an EIA employing anti-OCIF polyclonal antibodies.

Figure 14 shows a standard curve determining OCIF protein concentration by an EIA employing anti-OCIF monoclonal antibodies.

Figure 15 shows the effect of rOCIF protein on osteoporosis.--;

Page 5, Line 15, delete "procedure includes" and insert --procedures include--;

Line 16, delete "lyophilization" and insert --lyophilization--; delete "procedure includes" and insert --procedures include--;

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N.E.-

Line 21, delete the line in its entirety and insert --fibroblasts used for the production of OCIF protein are preferably IMR-90 cells. A--; and

Line 22, delete “the”.

Page 6, Line 1, delete “, using” and insert --in--;

Line 2, delete “for the cell culture”;

Line 4, delete “preferably” and insert --preferably--;

Line 5, before “purification steps of OCIF protein.” and insert --protein purification procedure.--

Line 6, before “OCIF” insert --The--; delete “initially obtained” and insert --obtained initially--;

Line 7, delete “heparin binding basic” and insert --basic heparin binding--; delete “basic”;

Line 9, delete “then by”;

Line 10, before “non-” insert --the--;

Line 13, delete the period “.” and insert a comma --,--; before “Cibacrone”
insert --a--;

Line 14, delete “Elmer) and” and insert --Elmer).--;

Line 15, delete the line in its entirety.

Line 17, delete “method of” and insert --method for--;

Line 18, delete “protein that inhibits differentiation and/or” and insert --protein.--; and

Line 19, delete “maturation of osteoclasts.”.

Line 18, delete "By using" and insert --Using--; delete "concentrations" and insert --concentration--;

Line 19, delete "blood and" and insert --blood,--; delete "cells-culture" and insert --cell-culture--;

Line 21, delete the line in its entirety;

Line 22, delete the line in its entirety; and

Line 23, delete the line in its entirety.

Page 9, Line 1, delete the line in its entirety;

Line 3, delete "to" and insert --for--; delete "determine" and insert --determining--;

Line 5, delete "the";

Line 6, delete "method" and insert --methods--;

Line 8, delete "using" and insert --transfected with--;

Line 9, delete "synthesized peptides designed" and insert --synthetic peptides--;

Line 11, delete "immunization of mammals" and insert --immunizing mammals such as mice or rats--;

Line 12, delete "myeloma of mammals" and insert --mammalian myeloma cells--;

Line 13, delete "hybridoma." and insert --hybridomas.--; delete "antibody" and insert --antibodies--; delete "recognizes" and insert --recognize--;

Line 14, delete the line in its entirety and insert --OCIF were selected and cultured to obtain the desired antibodies.--;

Line 15, delete the line in its entirety;

Line 16, delete the line in its entirety;

Line 17, delete the line in its entirety and insert --For immunizations, OCIF is suitably diluted with--;

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N.E.

Line 13, delete "ingredients" and insert --ingredient--; after "in" insert --bone diseases--;

Line 14, delete "bone diseases such as"; delete "osteoarthritis," and insert --osteoarthritis--;

Line 15, delete "The";

Line 16, delete "to establish" and insert --in the--; delete "the" and insert --bone--;

Line 17, delete "the"; delete "ingredients" and insert --ingredient--;

Line 19, delete "efficacious" and insert --effective--; and

Line 20, delete "human" and insert --humans--; delete "the".

Page 12, Line 1, delete "the" and insert --a--; delete "efficacious" and insert --effective--;

Line 2, before "pharmaceutically" insert --a--; delete "carriers." and insert --carrier.--;

Line 4, after "compounds" insert a comma --,--;

Line 6, delete the line in its entirety and insert --activators for injection, pH adjusters, buffers, stabilizers,--;

Line 7 - Line 23: delete the lines in their entirety.

Page 13, Delete the page in its entirety.

Page 14, Line 1 to Line 19, delete the lines in their entirety.

Line 22, delete "however," and insert --though--; delete "to the" and insert --thereto.--; and

Line 23, delete "examples."

Page 15, Line 6, delete "under" and insert --in--;

Line 9, delete the comma ",";

Line 18, after "from" insert --a--;

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Line 15, delete the line in its entirety and insert --activity, were pooled and designated sample 4.--;

Line 17, delete "fraction from" and insert --fractions--;

Line 18, after "to" insert --a--; and

Line 21, after "with" insert --a--.

Page 18, Line 1, delete "was" and insert --were--;

Line 2, delete "was" and insert --, were--;

Line 3, delete "was designated as" and insert --designated--;

Line 5, delete "was" and insert --were--;

Line 11, delete "The fractions number" and insert --Fractions--;

Line 12, after "NaCl" insert a comma --,--;

Line 14, delete "from 49 to" and insert --49 and--;

Line 17, delete "of" (second occurrence); after "with" insert --a--; and

Line 20, delete "peak 6 and the peak" and insert --peaks 6 and--.

Page 19, Line 11, delete "(6 and 7) with OCIF activity" and insert --with OCIF activity (peaks 6 and 7)--.

Page 20, Line 2, delete "were" and insert --are--;

Line 3, after "apparent" insert --molecular weight of--; delete "protein" and insert --sample--;

Line 7, delete "protein." and insert --sample.--; and

Line 14, delete "were" and insert --are--.

Page 21, Line 6, delete "No. 51-70 of blue-5PW fraction was" and insert --fractions 50 to 70 of the blue-5PW fractions were--;

Line 7, delete "was";

Line 8, delete "of";

Line 11, delete "peak 6 and peak" and insert --peaks 6 and--;

Line 12, delete "of" and insert --from--;

Line 14, delete "protein" and insert --proteins--; delete "N-terminal" and insert --the N-terminus--;

Line 15, delete "So, internal" and insert --Internal--;

Line 16, after "were" insert --therefore--;

Line 17, delete "of" and insert --from--; delete "peak 7" and insert --7,--; after "C4-HPLC" insert a comma --,--;

Line 20, after "each" insert --of the--; delete "mixture was" and insert --mixtures were--;

Line 21, delete "a"; after "Each" delete "the"; and

Line 22, delete "was".

Page 22, Line 3, after "vacuum" delete the comma --,--;

Line 10, after "with" insert --a--; after "gradient" insert --of--;

Line 13, delete "were" and insert --are--; delete "Sequence" and insert --SEQ. ID Nos. 1-3--;

Line 14, delete "Numbers 1-3";

Line 16, before "nucleotide" insert --the--;

Line 18, delete "by"; and

Line 19, after "using" insert --a--.

Page 23, Line 1, delete "sequence numbers" and insert --SEQ. ID Nos.--;

Line 2, after "2F" insert --(SEQ. ID No. 107)--;

Line 5, after "3R" insert --(SEQ. ID No. 108)--;

Line 14, delete “sequence number” and insert --SEQ. ID No.--;

Line 15, delete “the polypeptide.” and insert --OCIF.--;

Line 22, after “using” insert --a--; and

Line 23, after “using” insert --a--.

Page 26, Line 5, after “using” insert --a--;

Line 7, after “7-i)” insert a comma --,--; before “EcoRI” insert --An--;

Line 8, after "from" delete "the"; after "adaptor" insert --DNA--;

Line 11, delete “with the adaptor was inserted in” and insert --comprising the adaptor was legated into a--;

Line 12, after “at” insert --the--;

Line 13, after “using” insert --a--;

Line 14, delete “and” and insert --, yielding a--; delete “was prepared”;

Line 17, delete “infected to E. Coli,” and insert --used to infect E. coli strain--;

Line 19, delete “on the” and insert --onto--;

Line 21, after “(Amersham)” insert --membranes--; after “of” insert --the--; and

Line 22, delete “the”.

Page 27, Line 1, delete “the standard protocol” and insert --standard methods--; delete “on” and insert --onto--;

Line 2, after “in” delete “the”;

Line 5, before "denatured" insert --of--;

Line 8, delete “about 1.6 kb” and insert --a--;

Line 9, after "insert" insert --of about 1.6kb--;

Line 10, delete "and the infected into E. Coli" and insert --was used to infect E. coli strain--;

Line 11, delete "a" and insert --the--; delete "of" and insert --in the--;

Line 13, delete "1OCIF" and insert --λOCIF--;

Line 20, delete "picking up" and insert --lifting--;

Line 21, delete "to" and insert --in the--; and

Line 24, delete "transfered" and insert --transferred--.

Page 28, Line 2, delete "the standard protocol" and insert --standard methods--;

Line 7, after "using" insert --a--;

Line 8, after "T7" delete "primers";

Line 10, delete "sequence numbers" and insert --SEQ. ID Nos.--;

Line 11, delete "sequence number" and insert --SEQ. ID No.--;

Line 12, delete "sequence number" and insert --SEQ. ID No.--;

Line 16, after "pBKOCIF" insert a comma --,--; after "cDNA" insert a comma --,--;

Line 17, delete the commas (both occurrences) ",";

Line 18, after "electrophoresis" delete ",";

Line 19, after "using" insert --a--;

Line 20, delete the line in its entirety and insert --insert was ligated into the--;

Line 21, after "(Invitrogen)" insert --using DNA ligation kit ver. 2 (Takara Shuzo), and--; after "enzymes" delete ","; and

Line 22, delete "E. coli." and insert --E. coli strain--.

Page 29, Line 2, after "using" insert --a--;

Line 3, delete ",";

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Line 4, delete "was used in the experiments" and insert --for use in the experiments--;

Line 5, delete "the" and insert --OCIF--;

Line 6, delete the comma ",";

Line 7, before "prepared" insert an open paren --(--;

Line 8, delete "in" and insert --into--; delete "the" and insert --a--;

Line 11, delete the comma ",";

Line 12, delete " and were" and insert --,--;

Line 17, delete "the transfected cells were incubated" and insert --incubation--;

Line 20, delete "mice, 17 days-old," and insert --17 day old mice--;

Line 22, delete "D₃, and each" and insert --D₃ and a--; and delete "inoculatd" and insert --inoculated--.

Page 30, Line 5, delete "then";

Line 7, delete "The decrease of" and insert --A decrease in--; and

Line 8, delete "As result, the" and insert --The--.

Page 31, Line 4, delete "of";

Line 5, delete "with" and insert --using a--;

Line 6, delete "50 ml of a" and insert --a 50 ml--;

Line 9, after "with" insert --a--;

Line 10, after "and" insert --8 ml--; delete "(8 ml)";

Line 12, delete "OCIF active fraction (112 ml)" and insert --An OCIF active 112 ml fraction,--; after "NaCl" insert a comma --,--;

Line 18, after "with" insert --a--;

Line 19, delete a comma “,”; after “and” insert --0.5 ml--; delete (0.5 ml);

Line 22, delete “On SDS-PAGE under reducing conditions, a” and insert --A--; and

Line 23, delete “, under” and insert --by SDS-PAGE under reducing conditions.--.

Page 32, Line 1, delete “non-reducing conditions, bands” and insert --Bands--; delete “an apparent” and insert --apparent molecular weights of--;

Line 2, after “32” insert --under non-reducing conditions--;

Line 3, delete “fraction from” and insert --from fractions--;

Line 5, after “Lowry” insert a comma --,--;

Line 10, after “enzymes” delete the comma “,”;

Line 11, delete “an”; delete the comma “,”;

Line 12, after “using” insert --a--;

Line 14, delete the comma “,”;

Line 16, delete the comma “,”; after “using” insert --a--;

Line 18, after “using” insert --a--;

Line 19, after “using” insert --a--;

Line 20, delete “coli.” insert --coli strain--; and

Line 21, delete “The” and insert --A--.

Page 33, Line 1, after “of” insert --the--;

Line 3, delete “prepared in the” and insert --prepared in--;

Line 4, delete “the”;

Line 5, delete “method.” and insert --methods.--;

Line 6, delete “chrolide” and insert --chloride--;

Line 7, after “to” insert --the--;

Line 15, delete "to" and insert --into--;

Line 22, after "using" insert --a--; and delete "condition" and insert --the conditions--.

Page 34, Line 3, delete "Then the" and insert --The--; after "were" insert --then--;

Line 4, delete "in" and insert --into--;

Line 14, delete "the" and insert --a--; delete "amount" and insert --amounts--;

Line 15, after "OCIF," insert --named--;

Line 18, delete "the clone (5561)" and insert --clone 5561--; and

Line 20, delete "to".

Page 35, Line 2, delete "cells-conditioned" and insert --cell-conditioned--;

Line 3, delete "CHOcells-conditioned" and insert --CHO cell-conditioned--; delete "EXAMPL" and insert --EXAMPLE--;

Line 4, delete "of"; before "0.22" insert --a--;

Line 5, delete "Milipore" and insert --Millipore--;

Line 8, after "with" insert --a--;

Line 9, after "and" insert --8 ml--; delete "(8";

Line 10, delete "ml)";

Line 11, delete "Active" and insert --An active--;

Line 13, delete "of";

Line 14, delete "a" and insert --an--;

Line 17, after "with" insert --a--;

Line 18, delete the comma ",";

Line 19, delete "was" and insert --were--;

Line 20, delete "On SDS-PAGE";

Line 21, delete “a” and insert --A--; after “with” insert --an--; after “apparent” insert -
-molecular weight of--;

Line 22, delete “, under non-reducing conditions, bands” and insert --using SDS-PAGE under reducing conditions. Bands--;

Line 23, after “apparent” insert --molecular weights of--; and before “were” insert --using SDS-PAGE under non-reducing conditions--.

Page 36, Line 1, after “fraction,” insert --from fractions--;

Line 3, delete “obtained when” and insert --obtained, as--.

Page 37, Line 8, delete “sequence No.” and insert --SEQ. ID No.--;

Line 9, delete “the 22th amino” and insert --glutamine, located at position 22--;

Line 10, delete the line in its entirety and insert --from the translation start Met, as shown in SEQ. ID No.--;

Line 11, delete “number”;

Line 13, delete "was undetectable." and insert -- could not be determined.--;

Line 14, delete “converting from” and insert --the conversion of--;

Line 15, delete the line in its entirety and insert --cell culture or purification steps--;

Line 18, delete “from” and insert --in--;

Line 20, delete “sample was” and insert --samples were--; and

Line 23, delete “in” and insert --of a--.

Page 38, Line 1, delete “mice, 17 days-old,” and insert --17 day old mice--;

Line 2, delete “to” and insert --into--; delete “in” and insert --of a--;

Line 4, delete “a” and insert --an--; delete “mesuring” and insert --measuring--;

Line 5, delete "The" and insert --A--;

Line 11, delete "of" and insert --in--;

Line 16, before "molecular" insert --the--;

Line 14, delete “sequence number” and insert --SEQ. ID No.--;

Line 15, delete “the sequence number” and insert --SEQ. ID No.--;

Line 16, delete “the sequence number” and insert --SEQ. ID No.--;

Line 17, delete “the sequence number” and insert --SEQ. ID No.--;

Line 18, delete “the sequence number” and insert --SEQ. ID No.--;

Line 20, delete “the sequence number” and insert --SEQ. ID No.--; after “shown in” delete “the”;

Line 21, delete “sequence number” and insert --SEQ. ID No.--;

Line 22, delete “the sequence number” and insert --SEQ. ID No.--; and

Line 23, after “and are” insert --briefly--; and delete “in brief”.

Page 47, Line 1, before "OCIF2" insert --The--;

Line 2, after “in” insert --the--;

Line 2, delete “sequence number” and insert --SEQ. ID No.--;

Line 3, after “Accordingly” insert a comma --,--;

Line 5, delete “sequence number” and insert --SEQ. ID No.--;

Line 7, before "OCIF3" insert --The--;

Line 7, after “in” insert --the--;

Line 8, delete "sequence number" and insert --SEQ. ID No.--;

Line 9, after “Accordingly” insert a comma --,--; after “and” insert --an--;

Line 10, delete “sequence number” and insert --SEQ. ID No.--;

Line 11, delete “have” and insert --has--;

Line 12, delete “secreted” and insert --secretion of--;

Line 13, after “in” insert --the--;

Line 13, delete "sequence number" and insert --SEQ. ID No.--;

Line 15, after “Accordingly” insert a comma --,--;

Line 17, delete “sequence number” and insert --SEQ. ID No.--;

Line 19, after “in” insert --the--;

Line 19, delete “sequence number” and insert --SEQ. ID No.--;

Line 21, after “in” insert --the--;

Line 21, delete “sequence number” and insert --SEQ. ID No.--;

Line 23, after “Accordingly” insert a comma --,--; and

Line 24, after “sequence number” insert --SEQ. ID No.--.

Page 48, Line 4, delete “which is the” and insert --comprising--; after “of” insert --the--;

Line 5, after “in” insert --the--; delete “sequence” and insert --SEQ. ID No.--;

Line 6, delete “number”;

Line 7, after “Accordingly” insert a comma --,--;

Line 8, delete “sequence” and insert --SEQ ID No. 5).--;

Line 9, delete the line in its entirety.

Line 11, before “OCIF5” (first occurrence) insert --The--; before “OCIF” (second occurrence) insert --the--;

Line 12, delete “sequence number” and insert --SEQ. ID No.--;

Line 13, after “Accordingly” insert a comma --,--; after “and” insert --an--;

Line 14, delete “sequence number” insert --SEQ. ID No.--;

Line 15, delete “have” and insert --has--;

Line 16, delete “secreted” and insert --secretion of--;

Line 17, before "OCIF5" insert --The--;

Line 18, delete “sequence number” insert --SEQ. ID No.--;

Line 20, after "Accordingly" insert a comma --,--;

Line 21, delete "sequence" and insert --SEQ. ID No.--; and

Line 22, delete "number 5).".

Page 49, Line 3, delete "The Plasmid" and insert --Plasmids--; delete "was" and insert --were--;

Line 5, delete the comma ",";

Line 6, delete the comma ",";

Line 7, after "using" insert --a--;

Line 8, after "using" insert --a--;

Line 10, delete the comma ","; delete "coli." and insert --coli strain--;

Line 13, delete the comma ",";

Line 14, delete "an";

Line 15, after "using" insert --a--;

Line 16, after "using" insert --a--;

Line 17, delete "the" and insert --an--;

Line 18, delete the comma ","; after "E. coli" insert --strain--;

Line 21, delete "was"; after "with" insert --the--; delete the comma ","; and

Line 23, delete the comma ","; and after "using" insert --a--.

Page 50, Line 1, after "with" insert --the--; delete the comma ",";

Line 5, delete "an"; delete the comma ","; after "using" insert --a--;

Line 7, after "using" insert --a--; delete "E. coli." and insert --E. coli strain--;

Line 9, delete "obtained transformants" and insert --transformants obtained--; delete "variants" and insert --variant--;

Line 11, delete "column" and insert --columns--;

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Line 11, delete “variants” and insert --variant--;

Line 13, delete “experiments” and insert --experiments--;

Line 16, delete “plasmid,” and insert --plasmids--;

Line 17, delete “prepared”; and

Line 20, delete “a”.

Page 51, Line 5, delete “a”;

Line 5, before “DNA” insert --A--;

Line 7, after “using” insert --a--;

Line 12, before “DNA” insert --A--;

Line 13, after “using” insert --a--;

Line 14, delete “The” and insert --This--;

Line 16, delete “of” (second occurrence) and insert --from a--;

Line 18, delete “for” and insert --in--;

Line 20, after “E. coli” insert --strain--;

Line 21, delete “was” and insert --were--;

Line 22, delete “to the cells”;

Line 23, delete “was added”; and after “NaCl” insert --was added to the cells--;

Page 52, Line 3, delete “individually” and insert --each--;

Line 4, delete “each”;

Line 4, delete “of” (second occurrence);

Line 10, after “with” insert --a--; and

Line 14, after “with” insert --a--.

Page 53, Line 13, delete “SEQUENCE NO:” and insert --SEQ. ID Nos.--;

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Line 14, delete “as follows”;

Line 16, after “min” (first occurrence) insert a comma --,--;

Line 18, delete “size” and insert --sizes--;

Line 18, delete “prodcts was” and insert --products were--;

Line 19, delete “using” and insert --of the--; delete “solution” and insert --solutions--;

and

Line 20, after “using” insert --an--.

Page 54, Line 16, delete “size” and insert --sizes--; delete “products was” and insert --products were--; and

Line 19, delete “mutation” and insert --mutations--.

Page 55, Line 7, delete “was” (second occurrence) and insert --were--;

Line 9, delete “with” and insert --using a--;

Line 11, delete “as”;

Line 12, delete “of” (fourth occurrence) and insert --from a--;

Line 13, after “and” insert --the--;

Line 14, delete “E. coli DH5 α ” and insert --E. coli strain DH5 α --;

Line 16, delete “a”;

Line 19, delete “which is”;

Line 21, delete “with” and insert --using a--; and

Line 24, delete “of” and insert --from a--.

Page 56, Line 1, after "and" insert --the--;

Line 1, after “E. coli” insert --strain--;

Line 3, delete “a” (second occurrence);

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Line 8, delete “with” and insert --using a--;

Line 10, delete “as”;

Line 11, delete “of” and insert --from a--;

Line 12, after “and” insert --the--;

Line 12, after “E. coli” insert --strain--;

Line 14, delete “a” (second occurrence);

Line 19, delete “with” and insert --using a--;

Line 21, delete “was” (second occurrence) and insert --were--; and

Line 23, delete “with” and insert --using a--.

Page 57, Line 2, delete “of” (fourth occurrence) and insert --from a--;

Line 3, after “and” insert --the--;

Line 4, after “E. coli” insert --strain--;

Line 6, delete “a”;

Line 13, delete “with” and insert --using a--;

Line 15, delete “was” (second occurrence) and insert --were--;

Line 17, delete “with” and insert --using a--;

Line 20, delete “of” (fourth occurrence) and insert --from a--;

Line 21, after “and” insert --the--;

Line 22, after “E. coli” insert --strain--; and

Line 23, delete “a” (second occurrence).

Page 58, Line 10, delete “a”;

Line 10, delete "was" and insert --were--;

Line 16, delete “of” (second occurrence) and insert --from a--;

Line 17, after "and" insert --the--;

Line 18, after "coli" insert --strain--; and

Line 22, delete "plasmide" and insert --plasmids--.

Page 59, Line 4, delete "of" (second occurrence);

Line 6, delete "and" and insert --or--;

Line 7, delete "SEQUENCE NO:" and insert --SEQ. ID No.--;

Line 12, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--; and

Line 12, after "40-53" delete the comma --,--.

Page 60, Line 2, delete "fragment" and insert --fragments--;

Line 6, delete "which is";

Line 8, delete "with" and insert --using a--;

Line 10, delete "was" (second occurrence) and insert --were--;

Line 12, delete "with" and insert --using a--;

Line 15, delete "of" (third occurrence) and insert --from a--;

Line 16, after "and" insert --the--;

Line 17, after "E. coli" insert --strain--;

Line 18, delete "a" (second occurrence);

Line 23, delete "with" and insert --using a--;

Page 61, Line 1, delete "as" (first occurrence);

Line 3, after "and" insert --the--; after "E. coli" insert --strain--;

Line 6, delete "DNA ." and insert --DNA.--;

Line 10, delete "with" and insert --using a--;

Line 12, delete "as";

Line 13, delete “of” and insert --from a--;

Line 14, after “and” insert --the--; after “E. coli” insert --strain--; and

Line 21, delete “with” and insert --using a--.

Page 62, Line 2, delete “as”; delete “was” (second occurrence) and insert --were--;

Line 4, delete “with” and insert --using a--;

Line 6, delete “as”;

Line 8, delete "of" and insert --from a--;

Line 8, after “and” insert --the--;

Line 9, after “E. coli” insert --strain--; and

Line 11, delete “a”;

Line 16, delete “with” and insert --using a--;

Line 19, delete “of” and insert --from a--;

Line 20, after “and” insert --the--;

Line 20, after “E. coli” insert --strain--; and

Line 22, delete “a” (second occurrence).

Page 63, Line 3, delete “with” and insert --using a--;

Line 6, delete “of” and insert --from a--;

Line 7, after “and” insert --the--;

Line 7, after "E. coli" insert --strain--;

Line 9, delete “a” (second occurrence); and

Line 15, after “containing” insert --the--.

Page 64, Line 1, delete "of" and insert --from a--;

Line 1, after “and” insert --the--;

[illegible]

Line 2, after "E. coli" insert --strain--;

Line 4, delete "a" (second occurrence);

Line 12, delete "of";

Line 15, delete "SEQUENCE NO:" and insert --SEQ. ID No.--; and

Line 20, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--.

Page 65, Line 3, delete "with" and insert --using a--;

Line 5, delete "as";

Line 7, delete "of" and insert --from a--; after "and" insert --the--;

Line 8, after "E. coli" insert --strain--;

Line 10, delete "a";

Line 12, after "pSK-OCIF-CL" insert a period --.;

Line 13, after "PCR" insert --reaction--; and

Line 15, after "OCIF-CCR3" insert --were as follows:--.

Page 66, Line 3, delete "with" and insert --using a--;

Line 6, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--;

Line 12, delete "an";

Line 14, delete "The size of the PCR products was confirmed on an agarose gel.";

Line 15, after "using" insert --an--; and

Line 21, after "containing" insert --the--.

Page 67, Line 3, delete "CC R3" and insert --CCR3--;

Line 14, delete "isolatedand" and insert --isolated and --;

Line 16, delete "of" (second occurrence);

Line 18, delete "of" (second occurrence) and insert --from a--;

Line 19, after "and" insert --the--; and

Line 19, after "E. coli" insert --strain--.

Page 68, Line 1, after "in" (first occurrence) insert --the--;

Line 2, after "plasmid," insert --the--; delete "were" and insert --was--;

Line 7, delete "truncation" and insert --truncations--;

Line 8, delete "truncation" and insert --truncations--;

Line 9, delete "truncation" and insert --truncations--; before "OCIF" insert --An--;

Line 10, delete "of"; delete "are" and insert --were--;

Line 11, delete "of Leu-Val" and insert --(Leu-Val)--; before "OCIF" insert --An--;

Line 12, delete "of" (first occurrence); delete "are" and insert --were--; delete "of Ser-Leu-Asp" and insert --(Ser-Leu-Asp)--;

Line 13, before "OCIF" insert --An--; delete "of";

Line 14, delete "are" and insert --were--; delete "OCIF muatant" and insert --An OCIF mutant--;

Line 15, delete "of" (first occurrence); delete "are" and insert --were--; delete "of Leu-Val" and insert --(Leu-Val)--;

Line 17, delete "SEQUENCE NO:" and insert --SEQ. ID No.--;

Line 18, delete "was" and insert --were--; delete "one of the";

Line 19, delete "restriction enzymes,"; delete ", and" and insert --or--;

Line 20, delete ", and";

Line 21, delete "Ends" and insert --The ends--;

Line 22, after "in" (second occurrence) insert --a--; and

Line 23, delete "volumes" and insert --volume--.

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Page 69, Line 2, delete "of" and insert --from a--;

Line 4, after "E. coli" insert --strain--;

Line 8, delete "for";

Line 9, delete "pSK-OCIF- CSph" and insert -- pSK-OCIF-CSph--;

Line 10, delete "of";

Line 11, after "containing" insert --the--;

Line 13, delete "contain" and insert -- contained--; delete "pSK-OCIF- CSph" and insert --pSK-OCIF-CSph--;

Line 14, delete "and" and insert --or--; delete "as";

Line 18, delete "of" (second occurrence) and insert --from a--;

Line 19, after "and" insert --the--;

Line 20, after "coli" insert --strain--;

Line 22, after "which " insert --the--;

Line 23, please delete "is" and insert --was--; and

Line 25, delete "and" and insert --or--.

Page 70, Line 3, delete "Preparation" and insert --Preparation--; after "(" insert --a--;

Line 5, after "by" insert --using--; delete "column" and insert --columns--;

Line 13, delete "A 24-well plate was used for the DNA";

Line 14, delete "transfection.";

Line 15, delete "the" and insert --a 24 well--;

Line 17, delete "Mixture of an" and insert --A mixture of the--;

Line 19, delete "a CO₂ incubator" and insert --5% CO₂--;

Line 21, delete "48 more" and insert --a further 48--; delete "the CO₂ incubator" and insert --5% CO₂--;

Line 22, delete "for assay" and insert --in assays--;

Line 23, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--; and

Line 24, delete "SEQUENCE NO:" and insert --SEQ. ID No.--.

Page 71, Line 2, delete "Antigen" and insert --The Antigen--;

Line 3, delete "specific" and insert --the--; and

Line 4, delete "the" and insert --each--; delete "the".

Page 72, Line 4, after "OCIF" insert a semicolon -;--;

Line 5, after "50%" please insert a semicolon -;--;

Line 7, after "activity" insert a period --.;

Line 8, delete "western" and insert --Western--;

Line 10, delete "the" and insert --each--;

Line 11, delete "bromo phenol" and insert -- bromophenol --;

Line 12, after ")" insert a comma --,--; delete "a"; delete "polyacryl amide" and insert --polyacrylamide--;

Line 16, delete "peroxidase labeled" and insert -- peroxidase-labeled --;

Line 18, after "using" insert --an--;

Line 20, after "exclusively" insert --a--; after "for" insert --the--; and

Line 21, after "CC" insert --mutants--; delete "an".

Page 73, Line 3, delete "resare" and replace with "residues are";

Line 4, delete "SEQUENCE NO:" and insert --SEQ. ID No.--.

Page 74, Line 5, delete "purchased from STRATAGENE" and insert --(Stratagene)--;

Line 8, delete “also were” and insert --were also--;

Line 11, delete “on” and insert --onto--;

Line 16, delete “successively for one minute each” and insert --each one--;

Line 17, after “7.5)” insert --, successively for one minute--; delete “wet” and insert -- wetted--; and

Line 19, delete “on” and insert --onto--; delete “in” and insert --using a--.

Page 75, Line 7, delete “PFOTO” and insert --pFOTO--; and

Line 13, delete “on” and insert --onto--.

Page 76, Line 8, delete "the";

Line 10, delete “the”;

Line 13, delete “determination of the” and insert --determining their--;

Line 14, delete the comma “,”;

Line 15, delete “these from” and insert --therefrom--;

Line 16, delete “pairs” and insert --pair--; after “using” insert --a--; and

Line 20, after “(STRATEGENE)” insert a comma --,--.

Page 77, Line 3, after “and” insert --a--; delete “of”;

Line 5, delete "in" and insert --into--;

Line 8, delete "in" (second occurrence) and insert --into a--;

Line 11, delete “applied” and insert --separated--;

Line 11, delete “in” and insert --into--;

Line 15, delete “pBS6 H1.1” and insert -- pBS6H1.1--;

Line 17, after “using” insert --a--;

Line 18, after "and" insert --a--;

[illegible]

Line 23, after “Nucleotide” insert --The nucleotide--; delete “was” and insert --is--;
and

Line 24, delete “Sequence No” (first occurrence) and insert --SEQ. ID No.-- delete “Sequence No” (second occurrence) and insert --SEQ. ID No.--.

Page 78, Line 2, delete “of nucleotides”; delete “sequence” and insert --SEQ. ID--;

Line 3, delete “sequence” and insert --SEQ. ID No.--;

Line 8, delete “for” and insert --in--; delete “Three male JW rabbits (Kitayama”;

Line 9, delete “the line in its entirety and insert --For--;

Line 10, after "immunization," insert --an--;

Line 11, delete “The” and insert --Three--;

Line 12, delete “the interval of”; after “week” insert --intervals--;

Line 13, delete "The rabbits were injected six times at the interval";

Line 14, delete “of seven days subcutaneously”;

Line 15, delete “separated” and insert --isolated--;

Line 17, delete "40 w/v %," and insert --40% w/v, the--;

Line 18, delete “. Precipitate” and insert --The precipitate--;

Line 20, delete “resulting” and insert --resultant--;

Line 22, delete "Elutes were" and insert --The eluate was immediately--; and

Line 23, delete “immediately and were” and insert --and--.

Page 79, Line 2, delete “peroxidase labeled” and insert --peroxidase-labeled--; after “using” insert --an--;

Line 6, delete “separated by” and insert --separated using a--;

Line 6, delete "Protein pool" and insert --The protein pool was--;

Line 7, delete "maleimide activated" and insert --maleimide-activated--; delete "was"
and insert --and--;

Line 12, delete "4C" and insert --4°C--;

Line 14, delete "of";

Line 16, delete "peroxidase labeled" and insert -- peroxidase-labeled --;

Line 17, delete "temperture" and insert --temperature--; and

Line 21, delete "standared" and insert --standard--; delete "was" and insert --is--.

Page 80, Line 2, after "of" insert --a--;

Line 3, after "from" insert --the--; delete "fibroblasts" and insert --fibroblast--;

Line 4, after "IMR-90" insert --cells--;

Line 4, delete "Eample" and insert --Example--;

Line 6, delete "administrating" and insert --administering--;

Line 7, after "emulsion" insert --was--;

Line 8, delete "was administered"; delete "administration" and insert --
immunization--;

Line 9, delete "taken out," and insert --removed and--;

Line 10, delete "were";

Line 11, delete "the conventinal method" and insert --conventional methods--;

Line 12, delete "hybridoma" and insert -- hybridomas--; delete "Subsequently, to
check";

Line 13, delete "whether the selected hybridomas produce anti-OCIF antibody," and
insert --The presence of--;

Line 14, delete "each" and insert --the--; delete "hybridomas" and insert --each hybridoma--; delete "which" and insert --. Briefly,--;

Line 15, delete "was prepared by coating"; delete "in" and insert --of a--; delete "immunoplates" and insert -- immunoplate--; after "(Nunc)" insert --was coated--;

Line 16, delete "by blocking each well" and insert --blocked--;

Line 18, after "by" insert --by limit dilution--; delete "by limit dilution";

Line 19, delete "screening using the above"; delete ". Among thus obtained" and insert --screening--;

Line 20, delete the line in its entirety and insert --Several hybridoma clones producing high levels of anti-OCIF--; and

Line 23, delete ", which was".

Page 81, Line 1, delete the comma ","; delete "to" and insert --into--;

Line 2, after "(Aldrich)" insert a comma --,--;

Line 3, delete "the transplantation and the ascites containing" and insert --transplantation, thereby obtaining--;

Line 4, delete "was obtained" and insert a period --.--;

Line 6, delete "maufacturer's" and insert --manufacturer's--; delete "That is" and insert --Briefly--;

Line 7, after "ascites" insert --fluid--; after "with" insert --an--;

Line 8, after "to" insert --a--; delete "the" (second occurrence);

Line 10, delete "obtained eluate" and insert --eluate obtained--;

Line 11, delete "obtained antibody" and insert --antibody thereby obtained--;

Line 13, after "of" insert --a--; delete "to" and insert --for--;

W.E.

that--;

Line 7, after “inhibits” insert --the--;

Line 8, delete “a” and insert --an--; delete “to produce” and insert --for producing--;

Line 9, delete “has an activity to inhibit” and insert --inhibits the--;

Line 11, delete “accompanying” and insert --accompanied by--; delete “to be used”;

and

Line 13, delete “microorgainsm” and insert --microorganism--.

Line 18, delete “administered OCIF” and insert --with OCIF administered--.

Line 3, delete “Decrease of” and insert --A decrease is--; delete “the animals of
groups” and insert --control animals--;

Line 5, delete “groups” and insert --group--; delete “animal” and insert --animals

Line 7, after “inhibits” insert --the--;

Line 8, delete “a” and insert --an--; delete “to produce” and insert --for producing--;

Line 9, delete “has an activity to inhibit” and insert --inhibits the--;

Line 11, delete “accompanying” and insert --accompanied by--; delete “to be used”;